DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 6/30/08 has been entered in full. Claims 1 and 5-14 are amended.

Claims 1-14 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (3/28/08).

The objection to the specification at pg 2 is *withdrawn* in view of Applicants' amendments to the specification.

The objection to the oath/declaration at pg 2 is *withdrawn* in view of Applicants' filing of a new declaration on 7/23/08.

The objection to claims 1 and 8-14 at pg 3 are *withdrawn* in view of Applicants' amendments to the claims.

The rejection of claims 7, 12 and 14 under 35 U.S.C. § 112, first paragraph at pg 3-5 for failing to provide enablement for the full scope of the claims is *withdrawn* in view of Applicants' amendments to the claims to limit the recited cells to "isolated cells".

The rejection of claim 11 under 35 U.S.C. § 112, first paragraph at pg 5-6 for failing to provide enablement is *withdrawn* in view of Applicants' amendments to the claim that change the method to a method of screening for modulation of activity rather than expression.

The rejection of claims 1-13 under 35 U.S.C. § 102(b) at 6-9 are *withdrawn* in view of Applicants' amendments to the claims that limit the claims to SEQ ID NO: 1 or 2.

New objections and/or rejections

Claim Objections

Claims 1 and 12-14 are objected to because of the following informalities:

(1) Claim 1 is objected to because "the sequence of nucleotides" referred to in the claim is not clear. Due to the degeneracy of the genetic code, multiple nucleotide

sequences can encode SEQ ID NO: 2. Thus, claim 1 should more accurately recite "An isolated nucleic acid molecule, comprising a sequence of nucleotides that encodes the rhesus monkey BRS-3 (rhBRS-3) protein as set forth in SEQ ID NO: 2". It is noted that this change would not result in any withdrawn rejections being reinstated.

(2) Claim 12, line 2 recites "...of binding to (rhBRS-3) comprising:" The term rhBRS-3 should not be in parenthesis. Furthermore, line 2 should clarify that rhBRS-3 is the rhBRS-3 protein (or polypeptide) rather than rhBRS-3 nucleic acid.

(3) Claim 13 uses the term "rhBRS-3 protein" (lines 4 and 6), but parent claim 10 uses the term "polypeptide" (line 2). The term should be consistent in the parent and dependent claims.

(4) Claim 14, line 2, should clarify that rhBRS-3 is the rhBRS-3 protein (or polypeptide) rather than rhBRS-3 nucleic acid.

Appropriate correction is required.

Claim Rejections - 35 USC § 101, utility

The following is a quotation of 35 U.S.C. § 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-14 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1-14 are directed to the following. Claims 1-7 are directed to an isolated nucleic acid molecule (SEQ ID NO: 1) encoding a rhesus monkey bombesin receptor subtype-3 (rhBRS-3) of SEQ ID NO: 2, and expression vectors and host cells comprising said nucleic acids. Claim 8 is directed to a subcellular membrane fraction comprising said protein. Claim 9 is directed to a method of expressing said protein. Claim 10 is directed an isolated protein comprising the sequence of SEQ ID NO: 2. Claims 11-14 are directed to methods of screening for compounds that bind to, or modulate the activity of, the protein of SEQ ID NO: 2.

The specification teaches that the polypeptide of SEQ ID NO: 2 is a rhesus monkey (*Macaca mulatta*) ortholog of the human bombesin receptor subtype-3 (BRS-3). Example 4 shows "functional expression" of the receptor by demonstrating intracellular calcium mobilization in response to an artificial bombesin variant (D-Tyr6,B-Ala11,Phe13,Nle14]Bombesin (6-14)(dY-bombesin)) that also activates human BRS-3.

The specification teaches that "[b]ombesin, bombesin-like peptides and related receptors participate in a diverse array of physiological processes. BRS-3 has been implicated in the regulation of neuroendocrine function and energy metabolism (Ohki et al. Nature 390: 165-69 (1997)). Mice lacking functional BRS-3 are hyperphagic and have a reduced metabolic rate, which leads to the development of obesity, hypertension and diabetes as adults. Additionally, bombesin-like peptides may contribute to the pathogenesis of some human carcinomas" (¶ 7 of the published application). The specification further teaches that "would be advantageous to identify additional mammalian genes encoding bombesin receptor subtypes in order to allow screening to identify novel bombesin receptor modulators that may contribute to the regulation of endocrine processes, metabolism, or the cell cycle" (¶ 8).

The specification appears to assert that the claimed rhBRS-3 protein has utility in that the monkey BRS-3 can be used in a method of screening for compounds that modulate the receptor activity, and due to the similarity to human BRS-3 (over 95%) these modulators can then be used to treat human physiological functions associated with the receptor, such as diseases including obesity, hypertension and cancer.

However, the relevant art teaches as of 2008, BRS-3 (also known as BB_3) remains an "orphan receptor" and that "the function of the BB_3 receptor in normal physiology and pathological conditions is largely unknown because the natural ligand is still not known" (pg 31 of Jensen et al, 2008. Pharmacological Reviews. 60: 1-42). Jensen et al teach that naturally-occurring agonists of the other bombesin receptors have extremely low affinity for BRS-3 (see Table 2 on page 8). Jensen further teaches that "[a]n important insight into possible BB_3 receptor function was provided by studies of BB_3 receptor knockout mice" which "developed mild obesity, associated with hypertension and impairment of glucose metabolism" (pg 31). However, Jensen teaches

only that this is a "possible" function and does not describe any evidence suggesting a similar role in humans, or that the knockout mice have a reasonable correlation with any particular human disease state. Jensen does not teach any human disease has been associated with a reduction in BRS-3 activity (such as would be mimicked by a BRS-3 knockout). Jensen states, "[a]t present there are no diseases in which activation or alterations of the BB_3 receptor have been shown to be involved" (pg 31-32). Furthermore, Jensen teaches that affinity of rat BRS-3 for the artificial bombesin ligand is much lower than human BRS-3 (pg 31), which suggests unpredictability in whether the receptor is involved in identical processes in primates (e.g., humans or monkeys) and rodents. Thus, even if an agonist or antagonist of rhBRS-3 is identified by the claimed screening assays, what specific and substantial utility could it be used for? Further research would be required to determine whether or not an agonist of rhBRS-3 activity could treat a particular disease (such as one or more forms of obesity, hypertension or cancer) in humans. As Jensen concludes, "all of these possibilities remain unproven at present" (pg 32).

Thus, the proposed use of the receptor variant to screen for binding or modulating agents of rhBRS-3 is not a substantial utility. A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. The specification describes (Example 4) screening assays in which the receptor can be used, but does not teach disclose or specify a specific disease that is associated with the receptor.

An assay that screens for a compound that modulates the activity of a receptor that has a stated correlation to a predisposition to the onset of a particular disease condition would be a practical use of the material. However, a method of screening with a material that has no particular correlation with a disease does not constitute a substantial utility. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility. A stated belief that a correlation exists between the channel and any number of diseases is not sufficient guidance to use the claimed polynucleotides to treat

and/or diagnosis a particular disease; it merely defines a starting point for further research and investigation.

In summary, the instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids, proteins, and methods of screening.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646